Dyspnea in Dying Patients

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SUMMARY

Dyspnea is common in terminally ill patients and is often fairly difficult to control. If specific causes cannot be identified or treated, general measures to relieve symptoms should be used. Nondrug measures (eg, discussion and explanation with the patient) and drug measures (eg, morphine) can be used to control the dyspnea, although side effects, such as sedation, can be problematic.

RÉSUMÉ

La dyspnée est un phénomène courant chez les patients en phase terminale et elle est souvent difficile à contrôler. Lorsqu'il s'avère impossible d'identifier ou de traiter l'étiologie spécifique, on devrait prévoir des mesures générales visant à soulager les symptômes. Les mesures non pharmacologiques (p. ex. explication et discussion avec le patient) et médicamenteuses (p. ex. morphine) peuvent être utiles pour contrôler la dyspnée bien que certains effets indésirables, telle la sédation, peuvent devenir problématiques.

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DYSPNEA IS A PATIENT'S SUBJECTIVE awareness of difficulty in breathing. It can be described as laboured breathing, tightness, air hunger, sensation of suffocation, or breathlessness. The patient is anxious and in severe cases has a sense of impending death. Physical signs, such as tachypnea, hyperpnea, and use of accessory muscles of respiration are usually associated with dyspnea, but occasionally signs of increased ventilatory effort do not result in significant dyspnea (eg, metabolic acidosis). Dyspnea in patients with terminal illness, in a palliative care setting, is often referred to as "terminal dyspnea."

Because no objective method of measuring dyspnea exists, the reported incidence in terminal patients varies. Very generally speaking, about 50% (up to 70% in one study) of patients with terminal cancer demonstrate dyspnea, and of those with lung cancer, about 70% have dyspnea.[3] The higher incidence of dyspnea in lung cancer patients is consistently noted in fairly large studies. One study of 381 patients found that 69% of lung cancer patients showed signs of dyspnea.[5] The National Hospice Study found 65% of lung cancer patients had dyspnea.[3] Although one would expect dyspnea in patients with lung cancer, almost 25% of patients with terminal illness have dyspnea unrelated to lung cancer or concurrent respiratory or cardiac disease.[3] General debility or other medical problems must also be considered.

Dyspnea tends to increase as patients approach death: eg, the incidence increased from 17% of patients at 4 weeks before death to 28% during the last week.[6] During the last week of life, 25% to 30% of patients have dyspnea as a significantly distressing symptom.[2,3,6] Unfortunately, dyspnea seems fairly difficult to control, often more difficult to control than pain. Dyspnea was the most common symptom uncontrollable without sedating the patient in one study.[7] And dyspnea has been referred to as "the most common severe main symptom" at death.[2]

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Pathophysiology

Dyspnea can be caused by increased ventilatory demand (fever, anxiety, anemia); decreased ventilatory capacity (obstruction, lung stiffness, loss of normal lung tissue, respiratory muscle dysfunction); or neural stimulation (intracranial pressure, stroke, tumour).[5] These processes act through stimulation of the brainstem respiratory centres by central and peripheral

chemoreceptors sensitive to increased P_{CO_2}, decreased P_{O_2}, or decreased pH levels; by peripheral neuroreceptors; or by cortical or thalamic effects.[4]

However, the degree of dyspnea is not necessarily related directly to the degree of stimulation of such receptors. Some suggest that the sensation of dyspnea or breathlessness depends on the perception of the degree of respiratory muscle effort, ie, efferent motor command signals.[8] Thus, if both intercostal muscles and diaphragm are paralyzed, there might not be a perception of dyspnea. Other theories have also been postulated.[9] As with pain and other symptoms, dyspnea has an affective or psychological component. It clearly is increased by depression, anxiety, etc.

Dyspnea in palliative care can be thought of as due to 1) known existing conditions (eg, chronic obstructive pulmonary disease, asthma, congestive heart failure, anemia); 2) an acute superimposed condition, usually of the respiratory system (eg, atelectasis, pulmonary embolus, pneumonia, acidosis); 3) directly as a result of the cancer (eg, obstruction of bronchus, replacement of normal lung tissue, lymphangitis carcinomatosa, phrenic nerve involvement, superior vena cava obstruction, pleural effusion, ascites); or 4) secondary to cancer therapy (eg, radiation fibrosis, pneumothorax, chemotherapy).[3,4] More often than not, several different factors contribute to a patient's dyspnea.

Management

If a specific cause of dyspnea can be identified, the usual treatments can be instituted, eg, bronchodilators for chronic obstructive pulmonary disease, diuretics for congestive heart failure, radiotherapy for tumour, transfusion for severe anemia. In palliative care one must also consider the appropriateness of investigations and treatment. For example, antibiotic treatment of pneumonia might or might not be consistent with the patient's wishes for treatment.

If a specific cause is not identified or treatable, then measures to relieve the symptoms of dyspnea should be considered. General measures include taking time to talk to the patient and explaining the problem and plans for symptom control and treatments. A cool draft from a fan or window is often helpful. Increased humidity can be beneficial. Breathing exercises, physical therapy, and postural drainage can be considered, although sometimes they are impractical because of the general condition of the patient. Reducing the physical exertions required of the patient is often fairly simple if explicitly reviewed. Expectorants or mucolytic agents (eg, nebulized acetylcysteine) are useful in selected cases.[4,10]

Opioids, usually morphine, can be used to control dyspnea in dying patients. Since the 19th century, opiates have been used to relieve symptoms of asthma, pneumothorax, and emphysema.[11] Morphine reduces the subjective sense of dyspnea. It reduces the respiratory centre response to stimulation by increased P_{CO_2} or decreased P_{O_2}, and respiratory rate decreases after morphine administration.[5] However, a decrease in ventilatory function might not be evidenced by blood gas levels. Studies have shown that opiates given to patients with chronic obstructive pulmonary disease resulted in decreased breathlessness, increased exercise tolerance, and no significant deterioration of blood gas levels.[10] Morphine relieves dyspnea without much change in respiratory rate or blood gas measurements.[12] It appears that oxygen consumption is decreased by morphine, perhaps by reducing anxiety, muscle tension, and restlessness.

Conversely, patients with relatively normal blood gas levels can have severe dyspnea (eg, in lymphangitis carcinomatosa), where morphine seems simply to "reset" the level of respiratory drive.[5] The increased respiratory rate and effort associated with dyspnea can be counterproductive (eg, increased dead space ventilation and decreased alveolar ventilation), so that the effect of morphine, reducing respiratory rate, can in these instances actually improve ventilatory function.[4]

Morphine should be taken by mouth if possible. If a patient is already receiving morphine for pain, the dosage is increased by 50%. If a patient is not already receiving morphine or another opioid, then morphine, 5 mg every 4 hours, can be started. Further titration of dosage is

based on response and degree of side effects. For example, the dosage can be increased to 10 mg every 4 hours the next day, and then to 15 to 20 mg every 4 hours if dyspnea persists (respiratory rate greater than 24 respirations/min can be used as a guide).[4] A similar, slightly more detailed, protocol aims to control dyspnea and uses as a respiratory rate guideline for maintenance 12 to 15 respirations/min.[13]

If oral morphine is not tolerated, subcutaneous morphine can be used with good response.[12] In more severe cases, an intravenous infusion can be used. One approach uses a 1- to 2-mg bolus every 5 to 10 minutes until the dyspnea is relieved. Then the infusion is maintained at an hourly rate at 50% of the cumulative bolus amount.[14] The dosage can be increased 25% every 24 hours, subject to side effects of the morphine, notably sedation. It seems better to use an additional bolus as needed for exacerbations of dyspnea, rather than increasing the infusion rate, unless there are many exacerbations within a 24-hour period.

If the infusion does cause sedation, it should be stopped until recovery and then restarted at 50% of the previous rate. Naloxone should be used very cautiously to reverse sedation, as it appears to result in acute return of dyspnea.

Other medications can also be used to provide symptomatic relief of terminal dyspnea. Diazepam, or similar anxiolytics, can be useful if anxiety is a large component of the dyspnea.[4] However, diazepam has been noted to increase breathlessness and reduce exercise tolerance in patients with airway obstruction.[15] Promethazine has been tried with some relief of dyspnea. Oxygen can be used, preferably by nasal prongs or light mask, but the benefits must be weighed against the inconvenience of the apparatus for the patient. Nebulized bupivacaine has been mentioned, directed at the J-receptors, and could be useful for lymphangitis carcinomatosa. Glucocorticoids are useful in some instances, eg, bronchospasm, edema, lymphangitis carcinomatosa, laryngeal stricture, superior vena cava syndrome.[5] Prednisone, 20 to 40 mg/day, or dexamethasone, 2 to 4 mg twice daily, can be used. At the terminal stage, atropine, 0.4 to 1.0 mg every 4 to 8 hours, can be used to dry up secretions and help reduce the "death rattle," which can be quite upsetting to the family.

Ethical issues

Like morphine used for controlling pain in palliative care, morphine used for controlling dyspnea prompts concern over whether the treatment hastens the patient's death. The general principles of treatment still apply: ie, the physician "may accept the risk that a patient may die during a particular treatment if more satisfactory treatment options are unavailable or undesirable, providing treatment has been discussed with the competent patient or guardian," as outlined in the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioural Research.[14]

However, because physicians have been taught that morphine is a respiratory depressant, its use in patients already dyspneic is counter-intuitive. And as dyspnea can be difficult to control, resulting in some degree of sedation, the effect of morphine is more evident than when used for pain control. It should be recalled, though, that the use of morphine for relief of terminal dyspnea does not necessarily result in deterioration of ventilatory function. Even if there are some adverse effects, the degree of distress to a patient with moderate to severe dyspnea is such that measures directed toward relief are easily justifiable. ■

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